

3. The method of claim 2, wherein said TNF inhibitor is encoded by a nucleic acid sequence selected from the group consisting of:

- (i) the DNA sequence as shown in Fig. 32 or a coding portion thereof;
- (ii) the DNA sequence as shown in Fig. 39 or a coding portion thereof;
- (iii) the DNA sequence as shown in Fig. 40 or a coding portion thereof;
- (iv) the DNA sequence as shown in Fig. 56 or a coding portion thereof;
- (v) the DNA sequence as shown in Fig. 68 or a coding portion thereof;
- (vi) a sequence which is degenerate in the coding regions or portions thereof of (i), (ii), (iii), (iv) and (v);
- (vii) a sequence which hybridizes to a sequence complementary to (i), (ii), (iii), (iv), (v) or (vi); and
- (viii) a sequence which is complementary to (i), (ii), (iii), (iv), (v), (vi) or (vii).

4. The method of claim 3 wherein said TNF mediated disease is selected from the group consisting of arthritis, bowel necrosis, cachexia, leukemias and septic shock.

5. DNA encoding a TNF inhibitor selected from the group consisting of:

- (i) the DNA sequence as shown in Fig. 32 or a coding portion thereof;
- (ii) the DNA sequence as shown in Fig. 39 or a coding portion thereof;
- (iii) the DNA sequence as shown in Fig. 40 or a coding portion thereof;

- (iv) the DNA sequence as shown in Fig. 56 or a coding portion thereof;
- (v) the DNA sequence as shown in Fig. 58 or a coding portion thereof;
- (vi) a sequence which is degenerate in the coding regions or portions thereof of (i), (ii), (iii), (iv) and (v);
- (vii) a sequence which hybridizes to a sequence complementary to (i), (ii), (iii), (iv), (v) or (vi); and
- (viii) a sequence which is complementary to (i), (ii), (iii), (iv), (v), (vi) or (vii).

6. A nucleic acid encoding a TNF inhibitor, said TNF inhibitor comprising an amino acid sequence selected from the group consisting of:

- (i) an amino acid sequence as shown in Figure 38 or a fragment thereof;
- (ii) an amino acid sequence as shown in Figure 56 or a fragment thereof;
- (iii) an amino acid sequence as shown in Figure 57 or a fragment thereof;
- (iv) an amino acid sequence as shown by residues 1 through 182 (40kDa inhibitor Δ53) in Figure 57 or a fragment thereof; and
- (v) an amino acid sequence as shown by residues 1 through 184 (40kDa inhibitor Δ51) in Figure 57 or a fragment thereof.

7. A TNF inhibitor which is non-glycosylated and has a molecular weight of about 18kDa.

8. A TNF inhibitor produced in a host cell not capable of glycosylation or a non-human host cell capable of glycosylation and encoded by a nucleic acid sequence comprising a sequence selected from the group consisting of:

- (i) the DNA sequence as shown in Fig. 32 or a coding portion thereof;
- (ii) the DNA sequence as shown in Fig. 39 or a coding portion thereof;
- (iii) the DNA sequence as shown in Fig. 40 or a coding portion thereof;
- (iv) the DNA sequence as shown in Fig. 56 or a coding portion thereof;
- (v) the DNA sequence as shown in Fig. 58 or a coding portion thereof;
- (vi) a sequence which is degenerate in the coding regions or portions thereof of (i), (ii), (iii), (iv) and (v); and
- (vii) a sequence which hybridizes to a sequence complementary to (i), (ii), (iii), (iv), (v), or (vi).

9. A TNF inhibitor produced in a host cell not capable of glycosylation or a non-human host cell capable of glycosylation, said TNF inhibitor comprising an amino acid sequence selected from the group consisting of:

- (i) an amino acid sequence as shown in Figure 38 or a fragment thereof;

- (ii) an amino acid sequence as shown in Figure 56 or a fragment thereof;
  - (iii) an amino acid sequence as shown in Figure 57 or a fragment thereof;
  - (iv) an amino acid sequence as shown by residues 1 through 182 (40kDa inhibitor Δ53) in Figure 57 or a fragment thereof; and
  - (v) an amino acid sequence as shown by residues 1 through 184 (40kDa inhibitor Δ51) in Figure 57 or a fragment thereof.
10. A composition comprising the TNF inhibitor of claim 8 in a slow release formulation.
11. A lyophilized powder comprising the TNF inhibitor of claim 8.
12. The lyophilized powder of claim 11, further comprising a pharmaceutically acceptable carrier.
13. A kit for preparing an aqueous pharmaceutical formulation comprising the lyophilized powder of claim 11 and a physiologically acceptable solvent.
14. A host cell containing a recombinant DNA molecule comprising a nucleic acid sequence defined in claim 5.
15. A process for preparing a recombinant TNF inhibitor polypeptide, comprising producing the recombinant TNF inhibitor polypeptide in a host cell according

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to claim 14 under suitable conditions to express the recombinant DNA molecule contained therein to produce the recombinant polypeptide.

16. ~~The process of claim 15, further comprising harvesting the TNF inhibitor.~~

17. A substantially purified interleukin-1 inhibitor (IL-1i), comprising a glycosylated or nonglycosylated polypeptide, said polypeptide being capable of inhibiting IL-1 and being sufficiently pure such that at least a portion of the amino acid sequence of said polypeptide can be determined, wherein said polypeptide is selected from the group consisting of

A) a polypeptide comprising all or an IL-1 inhibitory fragment of the amino acid sequence:

(U) (X) P S G R K S S K M Q A F R I W D V N Q K T F Y L R N  
N Q L V A G Y L Q G P N V N L E E K I D V V P I E P H A  
L F L G I H G G K M C L S C V K S G D E T R L Q L E A V  
N I T D L S E N R K Q D K R F A F I R S D S G P T T S F  
E S A A C P G W F L C T A M E A D Q P V S L T N M P D E  
G V M V T K F Y F Q E D E

wherein (U) is M or nothing and (X) is R or P; and

B) a polypeptide that is at least about 70% homologous to the amino acid sequence set forth in A).

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18. A composition comprising the IL-1 $\alpha$  of claim 17 in a slow release formulation.
19. A lyophilized powder comprising a polypeptide capable of inhibiting interleukin-1 (IL-1) and being sufficiently pure such that at least a portion of the amino acid sequence of said polypeptide can be determined, wherein said polypeptide is methionylated or non-methionylated and has an amino acid sequence that is at least 70% homologous to the following amino acid sequence:

(U) (X) P S G R K S S K M Q A F R I W D V N Q K T F Y L R N  
N Q L V A G Y L Q G P N V N L E E K I D V V P I E P H A  
L F L G I H G G K M C L S C V K S G D E T R L Q L E A V  
N I T D L S E N R K Q D K R F A F I R S D S G P T T S F  
E S A A C P G W F L C T A M E A D Q P V S L T N M P D E  
G V M V T K F Y F Q E D E

wherein (U) is M or nothing and (X) is R or P.
20. The lyophilized powder of claim 19, further comprising a pharmaceutically acceptable carrier.
21. A kit for preparing an aqueous pharmaceutical formulation comprising the lyophilized powder of claim 19 and a physiologically acceptable solvent.

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*An isolated nucleic acid sequence*

22. ~~An isolated nucleic acid sequence encoding an interleukin-1 inhibitor (IL-1i)~~

polypeptide, said polypeptide being capable of inhibiting IL-1, wherein said polypeptide is selected from the group consisting of

A) a polypeptide comprising all or an IL-1 inhibitory fragment of the amino acid sequence:

(U) (X) P S G R K S S K M Q A F R I W D V N Q K T F Y L R N  
N Q L V A G Y L Q G P N V N L E E K I D V V P I E P H A  
L F L G I H G G K M C L S C V K S G D E T R L Q L E A V  
N I T D L S E N R K Q D K R F A F I R S D S G P T T S F  
E S A A C P G W F L C T A M E A D Q P V S L T N M P D E  
G V M V T K F Y F Q E D E

wherein (U) is M or nothing and (X) is R or P; and

B) a polypeptide that is at least about 70% homologous to the amino acid sequence set forth in A).

23. ~~A host cell containing a recombinant DNA molecule comprising a nucleic acid sequence defined in claim 22.~~

24. ~~A process for preparing an interleukin-1 inhibitor (IL-1i) polypeptide, comprising producing the recombinant IL-1i polypeptide in a host cell according to claim 23 under suitable conditions to express the recombinant DNA molecule contained therein to produce the recombinant polypeptide.~~

25. The process of claim 24, further comprising harvesting the IL-1*i* polypeptide.
26. A composition comprising a water-soluble polymer comprising a reactive Michael acceptor.
27. A composition of claim 26, wherein said polymer further comprises a second reactive Michael acceptor or a reactive NHS-ester.
28. A composition of claim 26, wherein said Michael acceptor is maleimide.
29. A composition of claim 26, wherein said Michael acceptor is vinyl sulfone.
30. A composition of claim 26, wherein said polymer further comprises a reactive NHS-ester and wherein said Michael acceptor is maleimide.
31. A composition of claim 26, wherein said polymer further comprises a reactive NHS-ester and wherein said Michael acceptor is vinyl sulfone.
32. A composition of claim 26, further comprising a biologically-active molecule conjugated to said polymer.
33. A composition of claim 32, wherein the Michael acceptor is a sulfone moiety and said biologically-active molecule has a reactive thiol moiety, and wherein said sulfone moiety forms a linkage with said thiol moiety.
34. A composition of claim 33, wherein said sulfone moiety is vinyl sulfone.
35. A composition of claim 32, wherein said biologically-active molecule is a tumor necrosis factor (TNF) inhibitor.